REMARKS

In the present communication, Claims 27, 28, 30, 32, 35, 37, and 38 have been amended. Claims 7-40 are currently pending. The Examiner's objections and rejections are as follows:

I) The Examiner issued a restriction requirement with respect to Claims 8, 9, 11-15, 31-35, and 39;

II) The Examiner objected to certain formalities in the Figures;

III) The Examiner objected to various formalities in the Specification;

IV) The Examiner requested sequence identifiers in the Specification;

V) The Examiner objected to certain formalities in Claims 27 and 37;

VI) Claims 28, 30, and 38 were rejected under 35 U.S.C. 112, second paragraph, as allegedly indefinite;

VII) Claims 7, 10, 16-24, 26, 28, 30, 36, 38, and 40 were rejected under 35 U.S.C. 102(b) as allegedly anticipated by Lorincz et al. (US Pat. 6,136,535); and

VIII) Claims 25, 27, 29, and 37 were rejected under 35 U.S.C. 103(a) as allegedly obvious in view of Lorincz in view of Hall et al. (U.S. Pat. 5,994,069).

I. Restriction Requirement

The Examiner issued a restriction requirement with respect to Claims 8, 9, 11-15, 31-35, and 39. (Office Action, pages 2-5). The Examiner's reason for restricting all of these claims (except for Claim 13) is that these claims relate to generating a transcription substrate with a linear substrate, while the originally elected claims relate to generating a transcription substrate with a circular substrate. Applicants disagree with this restriction. Each of the currently pending claims requires that a circular substrate be formed and therefore are part of the elected group. In the claims identified by the Examiner, the method may further include creating a linear structure, but in every case, a circular substrate is formed. For example, dependent claim 8 invovles the step of linearizing the circular sense promoter-containing first-strand cDNA. In this case, a circular molecule was formed (the elected invention). The fact that an addition process step

occurs does not alter this point. If claim 8 were cancelled, claim 7, its independent claim would still need to be examined in the exact same manner. To the extent claim 7 is patentable around the prior art, by definition, so is claim 8, which incorporates all of the limitations of claim 7 (thus, at most, the restriction should be considered a species election, and the subject matter of all of the claims should be considered if the independent claims are otherwise found allowable). Applicants therefore believe that the restriction should be withdrawn. To the extent the Examiner wishes to maintain the restriction, Applicants request a phone interview to discuss the restriction.

II. Figures

The Examiner objected to certain formalities in the Figures. Applicants have included amended figures with this communication.

III. Specification

The Examiner objected to various formalities in the specification. The Examiner requested that the Title and Abstract be amended to reflect the subject matter of the claims. Applicants have made these amendment. The Examiner also requested that certain tradenames be capitalized in the specification. Applicants note that under MPEP 608.01(v), trademarks need to either be capitalized or "TM" or "®" needs to be indicated after the word. The specification already contains "TM" after the words cited by the Examiner. As such, Applicants submit that this objection should be withdrawn.

IV. Sequence Rule Compliance

The Examiner requested that the sequences on pages 4 and 33 of the specification be labeled with SEQ ID numbers. Applicants have labeled the sequences on these pages with SEQ ID numbers corresponding to the previously submitted sequence listing.

V. Formalities in Claims 27 and 37

The Examiner objected to listing "5-end" without using a " ' ." Applicants have amended these claims as suggested by the Examiner.

VI. Indefiniteness Rejection of Claims 28, 30, and 38

The Examiner rejected Claims 28, 30, and 38 under 35 U.S.C. 112, second paragraph, as allegedly indefinite. In regard to Claims 28 and 38, Applicants have deleted "RNA" and replaced this with "transcription product," as this is the product being referenced. In regard to Claim 30, Applicants have replaced "said target nucleic acid" with "a target RNA nucleic acid." As such, Applicants request that these indefiniteness rejections be withdrawn.

VII. Anticipation Rejection

The Examiner rejected Claims 7, 10, 16-24, 26, 28, 30, 36, 38, and 40 under 35 U.S.C. 102(b) as being anticipated by Lorincz et al. (US Pat. 6,136,535) (Office Action, page 10). However, the methods described in the Lorincz et al. reference are very different from the methods of the presently claimed invention.

First, Lorincz et al. does not teach the use of a sense promoter primer in any context. The methods described and illustrated in Lorincz et al. all use an anti-sense promoter primer or a probe that contains an anti-sense promoter sequence. Thus, the template strands that are transcribed using the methods described by Lorincz et al. are derived from the target DNA. In contrast, the method of the presently claimed invention uses a sense promoter primer. Claim 7 exemplifies the differences highlighted by two aspects: first, the sense promoter primer that is annealed to a target sequence is extended to synthesize first-strand cDNA; and second, the resulting first-strand cDNA that contains the *sense promoter primer* at its 5'-end is ligated to *itself* to form a circular single-stranded first-strand cDNA product. The promoter sequence in the promoter primer of Lorincz et al. are not joined directly to the 3'-end of the template strand that is transcribed by the RNA polymerase. This is illustrated by the fact that in the BRIEF DESCRIPTION OF THE DRAWING in column 4 of Lorincz et al., FIG 1C refers to the method "thereby producing a double-stranded DNA having a functional RNA polymerase promoter at its *5'-end.*" The methods of the presently claimed invention join the sense promoter sequence of the sense promoter primer to the *3'-end* of the first-strand cDNA extension product. It is further illustrated by the fact that the promoter sequence presented on the top of the page containing

columns 17 and 18 of Lorincz et al. is an *anti-sense promoter sequence*, not the obligatory *sense promoter sequence* of the *sense promoter primer* of the presently claimed invention.

As part of the rejection, the Examiner cites Lorincz as allegedly teaching that the first strand nucleic acid (transcription product) can be ligated to itself based on the following passage from Lorincz et al: "Optionally, a ligation reaction may be carried out to fill in the gap between the promoter and the template." (Office Action, page 11).

However, the only uses of a ligase or ligation described anywhere in Patent No. 6,136,535 for the method of Lorincz et al. were to join a *linear* promoter probe to a *linear* trimmed target DNA to obtain a *linear* transcription substrate (e.g., see FIG. 5 and FIG. 6 of Lorincz et al.).

A search of Lorincz et al. shows only the following additional statements related to use of a "ligase" or "ligation" in the methods of Lorincz et al. (none of which are of any relevance to the method of the present invention):

Lines 2-7, column 4: "Optionally, a ligation reaction may be carried out to fill the gap between the promoter and the template. Further, it may be desired to produce a fully double stranded transcription template by first extending the partially double stranded hybrid with a nucleotide polymerase, preferably a DNA polymerase."

Lines 52-65, column 6: "In one embodiment of ds-CAR, upon hybridization, the 3' end of the DNA target directly abuts the 5' end of the short strand of the ds-promoter-primer. This hybrid structure may be directly subjected to transcription. Optionally, ligase may then be reacted with this hybrid forming a continuous, partially double-stranded template which is also transcription-ready. Yet another optional step may include extending either of the above described partially double stranded molecules (either ligated or non-ligated) with a DNA polymerase, thereby producing a fully double stranded template, also ready for transcription (see, for example, Zhou, et al. 1995 Cell 82, 577-585). Transcription is then carried out using an RNA polymerase to produce many RNA transcripts."

Lines 43-46, column 11: "Transcription of the double-stranded extension product or partially double stranded ligation product carrying a functional promoter sequence is facilitated by an RNA polymerase."

Clearly, in no case did Lorincz et al. describe formation of a circular transcription substrate and none of the figures in Lorincz et al. shows a circularized probe molecule (nor

would circularization of any of the Lorincz et al. molecules fit within the claimed language as Lorincz does not employ a sense promoter primer). In contrast, circularization of the first-strand cDNA formed by extension of a sense promoter primer that is annealed to a target sequence is an element of the methods of the presently claimed invention.

In light of the lack of teaching of ligating the sense promoter-containing first-strand cDNA to itself, the Lorinz et al. reference does not anticipate the claims. Likewise, in light of the lack of teaching of forming a circular product via ligation, the Lorinz et al. reference does not anticipate the claims. Further, in light of the lack of teaching of use of a "sense promoter primer"[1] in any context (the promoter probe of Lorincz is an anti-sense promoter), the Lorinz et al. reference does not anticipate the claims. As such, this rejection should be withdrawn.

VIII. Obviousness Rejection

The Examiner rejected Claims 25, 27, 29, and 37 under 35 U.S.C. 103(a) as allegedly obvious in view of Lorincz in view of Hall et al. (U.S. Pat. 5,994,069) (Office Action, page 17). In light of the explanation regarding the teaching of Lorincz et al. presented above, Applicants submit that this obviousness rejection fails. For example, this combination of reference fails to teach where the promoter containing transcription product is ligated to itself. Therefore, Applicants request that this rejection be withdrawn.

---

[1] The specification explains that: As defined herein, the promoter sequence of a double-stranded promoter that is operably joined to the 3'-end of the template strand sequence that is transcribed is a "sense promoter sequence" and a promoter primer that comprises this sequence is "a sense promoter primer." The sequence of a double-stranded promoter that is complementary to the sense promoter is defined herein as "an anti-sense promoter" and a promoter primer that comprises this sequence is "an anti-sense promoter primer." (Specification, paragraph 164).

CONCLUSION

If the Examiner wishes to discuss this case, Applicants encourage the Examiner to call the undersigned at 608-218-6900 at the Examiner's convenience.

Dated: July 25, 2007

/ David Casimir /

David Casimir
Registration No. 42,395
MEDLEN & CARROLL, LLP
101 Howard Street, Suite 350
San Francisco, California 94105
608.218.6900